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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,841	11/17/2000	Roger Briesewitz	STAN-130	8223
24353	7590	03/11/2004	EXAMINER	
BOZICEVIC, FIELD & FRANCIS LLP			NAFF, DAVID M	
200 MIDDLEFIELD RD				
SUITE 200			ART UNIT	
MENLO PARK, CA 94025			PAPER NUMBER	
			1651	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/716,841

Applicant(s)

BRIESEWITZ ET AL.

Examiner

David M. Naff

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2003.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16, 17, 21-23, 26-28, 31, 32, 51, 52, 55-57, 60-62, 65 and 66 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 16, 17, 21-23, 26-28, 31, 32, 51, 52, 55-57, 60-62, 65 and 66 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Response to Amendment

The amendment of 12/18/03 amended claims 16, 21, 23, 26, 28, 31, 51, 55, 57, 60, 62 and 65, and canceled claims 19, 20, 24, 25, 29, 30, 53, 54, 58, 59, 63 and 64.

5 Claims examined on the merits are 16, 17, 21-23, 26-28, 31, 32, 51, 52, 55-57, 60-62, 65 and 66, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10 **Claim Rejections - 35 USC § 102**

Claims 16, 17, 21-23, 26-28, 31, 32, 51, 52, 55-57, 60-62, 65 and 66 are rejected under 35 U.S.C. 102(e) as being anticipated by Briesewitz et al (6,372,712 B1).

15 The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the
20 reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

25 The claims are drawn to modulating a pharmacokinetic property of a drug including half-life and hepatic first-pass metabolism of the drug by administering a bifunctional molecule of less than 5000

daltons molecular weight consisting of the drug and a pharmacokinetic modulating moiety, which may be jointed to the drug by a linker. As disclosed in the specification (pages 25-27), when modulating half-life and hepatic first-pass metabolism, the modulating moiety can be FK506 or rapamycin, the intracellular protein to which it binds is FKBP (peptidyl-prolyl isomerase), and the drug can be a thymidylate synthase inhibitor (AG337) or a dihydrofolate reductase inhibitor.

Briesewitz et al disclose administering to a host a bifunctional molecule of less than 5000 daltons molecular weight consisting of a drug moiety and a presenter protein ligand joined to the drug moiety. The drug moiety binds to a drug target and the presenter protein ligand binds to a presenter protein. The drug moiety exhibits at least one of enhanced affinity, specificity or selectivity for its target as compared to a free drug control. As disclosed in the specification (col 16, lines 12-41), the presenter protein can be FKBP and the ligand can be FK506 or rapamycin, and the drug can be an enzyme inhibitor such as an inhibitor of dihydrofolate reductase (col 33, lines 24-39). Also, see claims 1-15. In claim 6, the ligand binds to peptidyl prolyl isomerase.

The bifunctional molecule of Briesewitz et al can be the same as presently claimed, and administering the bifunctional molecule as disclosed by Briesewitz et al will inherently result in modulating of a pharmacokinetic property because of the drug moiety exhibiting enhanced affinity, specificity or selectivity for its target as compared to a corresponding free drug control.

Response to Amendment

Applicants have presented a 1.132 Declaration by Dr. Wandless stating that the three co-inventors of the instant invention are sole inventors of the subject matter disclosed by Briesewitz et al relied on in the rejection. However, the declaration should have been signed by all of three co-inventors. Additionally, it is not seen how the present co-inventors can be the sole inventor of subject matter of Briesewitz et al relied on since Briesewitz et al contains Ray and Vogel as additional co-inventors, and the claims of Briesewitz et al encompass a bifunctional molecule that can be the same required in the method of the present claims. Administering the bifunctional molecule as disclosed by Briesewitz et al will inherently result in modulating a pharmacokinetic property of a drug as results in the presently claimed method since the claims of Briesewitz et al require the drug to exhibit at least one of enhanced affinity, specificity or selectivity for its target as compared to a corresponding free drug control. The declaration should set forth the specific subject matter disclosed by Briesewitz et al that is invented by the present three co-inventors, and point out how this subject matter differs from the subject matter invented by the five co-inventors of Briesewitz et al.

Double Patenting

Claims 16, 17, 21-23, 26-28, 31, 32, 51, 52, 55-57, 60-62, 65 and 66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-29, 31-50, 52 and 53 of copending Application No. 10/025,936.

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Although the conflicting claims are not identical, they are not patentably distinct from each other because administering the bifunctional molecule of the claims of the copending application would have inherently modulated a pharmacokinetic property as presently
5 claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

The terminal disclaimer of 12/18/03 does not overcome the double
10 patenting rejection over application 10/025,936 since the Serial Number of the application is incorrect in the terminal disclaimer. The correct number is 10/025,936 and not 09/025,936. A new terminal disclaimer is required with the correct application number.

THIS ACTION IS MADE FINAL. Applicant is reminded of the
15 extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after
20 the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX
25 MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

5 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

10 Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see [http://pair-](http://pair-direct.uspto.gov)
15 [direct.uspto.gov](http://pair-direct.uspto.gov). Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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David M. Naff
Primary Examiner
Art Unit 1651

25 DMN
3/8/04